Remarks

The Office Action was electronically transmitted on December 3, 2007. In view of the amendment above and remarks below, reconsideration is respectfully requested.

While the Office Action raised indefiniteness, omitting essential steps, enablement and written description rejections, the underlying concerns appear to reflect just the following issues:

(a) whether fragments of the non-phosphorylated marker should continue to be included. The present application teaches the sequence of the non-phosphorylated marker protein. Further, paragraph [0023] of the application discloses that fragments can be used to develop polyclonal or monoclonal antibodies.

While Applicant therefore believes that the disclosure of the present application supports non-phosphorylated fragments, and how to develop antibodies to them, it appears that the Office's main concern regarding this inquiry is whether enough such fragments that are theoretically possible would be relevant to monitoring transplant rejection. Rather than addressing that issue here, and in order to help expedite allowance, the claims now render that concern moot by removing the non-phosphorylated fragments, without prejudice to the filing of a divisional.

(b) why there is no size range for the phosphorylated fragments. During the interview Applicant had understood that the Office had agreed that no such limitation was needed in view of the declaration to be submitted. In any event, to expedite allowance, a size range (consistent with original claim 14) is now included.

For example, in the AJT paper of record, applicant reported an experiment of using cut-offs at 50 and 100 kDa. With those cut-off sizes, the cited IkB fragment would have been excluded, regardless of its prevalence.

(c) how the method of monitoring fragments of the phosphorylated marker using antiphosphotyrosine antibody could successfully work, given the purported presence of unrelated phosphorylated tyrosine protein in kidneys within the size range. Applicant has several responses to this.

First, the record does not support the assertion that there are "many" kidney proteins within the size range where their tyrosine is phosphorylated. The record only establishes a single IkB protein that under certain conditions, via one of a variety of alternative pathways, sometimes becomes phosphorylated at a tyrosine position.

In any event, there is nothing of record to support the view that substantial quantities of that size phosphorylated IkB survive homogenation still within the size range. The issue isn't what is in natural kidney cells, it is what survives the homogenation. The Office Action did not even establish prima facie that phosphorylated tyrosine IkB survives homogenation in the size range at all, much less in substantial masking quantities.

Further, the fact that something might survive in quantities only visible under overexposure conditions does not destroy enablement. The actual experiments in the application, the declaration, and a peer-reviewed publication all support the unrebutted view that the background which can be seen under overexposure is not at a masking level during typical exposure.

In any event, phosphorylated IkB appears to increase with certain unusual conditions. There is no support in the record for it decreasing once created, much less decreasing under rejection conditions. Hence, there is nothing to establish that it even theoretically could suggest a false positive.

Most importantly, whatever presence this phosphorylated IkB protein (or other purported phosphorylated non-SBP-1 proteins

within the size range) may have in the homogenate is irrelevant since the evidence indicates that they don't alter their presence within the size range in response to rejection. As noted in the application, it is highly preferred to use a comparison to a known standard as a part of the method, which would wash out any such effect.

In sum, there is no evidence of a prevalence of numerous other phosphorylated tyrosine residue proteins within the relevant size range in kidneys, no evidence that any others survive the homogenation in substantial quantity within the size range, no evidence that any that survive interfere with the testing, and no evidence that comparison to known standards wouldn't in any event avoid any inaccuracies.

(d) whether the 20-80 kDa range is what was intended. Alteration of the homogenation conditions can alter slightly the size of the down regulated fragment within the range. Hence, the selected range was intentional, regardless of what specific results were reported in the article for a particular homogenation.

(e) whether antibodies can detect the <u>whole</u> marker proteins (as distinguished from the fragments). Paragraph [0023] describes the use of monoclonal and polyclonal antibodies for this purpose. Further, paragraphs [0061] - [0067] describe the development of antibodies to SBP-1. Consistent with the fact that they were developed from rabbit sera to the phosphorylated SBP-1, they also recognize the phosphorylated variant.

Conclusion

Hence, this application is now believed to be in condition for allowance. No additional fee is believed necessary for the consideration of the enclosed declaration and interview summary. However, if one is, please charge Deposit Account 17-0055 for the needed fees.

Respectfully submitted,

Majed M. Hamawy

Dated: January 28, 2008 By: _____

Carl R. Schwartz
Quarles & Brady LLP
411 East Wisconsin Avenue
Milwaukee, WI 53202
(414) 277-5715
Reg. No. 29,437

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